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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,613	09/26/2003	Gerd Dannhardt	104035.269169	3699

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EXAMINER	
COPPINS, JANET L	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 04/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/672,613	DANNHARDT ET AL.	
	Examiner	Art Unit	
	Janet L. Coppins	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2006*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7,12-15 and 21-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-3,5-7,12-15,22,24-30,32 and 34* is/are allowed.

6)☒ Claim(s) *21,23,31 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3, 5-7, 12-15, and 21-34 are pending in the instant application.

Priority

1. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany on March 26, 2001. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), on October 11, 2005, which papers have been placed of record in the file.

Response to Amendment

2. Receipt is acknowledged of Applicants' Amendment and Response, filed January 5, 2006, which has been reviewed by the Examiner. Accordingly, claim 6 has been amended, and new claims 31-34 have been added.

3. Regarding claims 28-30, drawn to cosmetic compositions and withdrawn in the previous Office Action, it is noted that the original Examiner on this case, Examiner Waller, had included cosmetic preparations in the elected Group I, which contains compounds of formula I. Therefore, claims 28-30 are herein rejoined for examination on the merits.

4. New claims 31-34, drawn to methods of use, are added to original Group II of the Restriction Requirement, which was rejoined in the previous Office Action for examination.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 21 and 23 previously rejected under 35 U.S.C. 112, first paragraph, as not being enabled. The specification, while being enabling for compounds according to formula (I) for

treating certain diseases that respond to the inhibition of cyclooxygenase, does not reasonably provide enablement for treating all of the diseases encompassed by the above claims. In the previous Office Action, Applicants' failure to meet the *In re Wands* factors were discussed.

Applicants traverse the rejection, arguing that, "the Office is overstating the requisite bounds for enablement and is focusing on breadth rather than considering all relevant factors. MPEP 2164.06 states that the test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed," (Applicants' Remarks, page 13). The Examiner respectfully disagrees, and maintains the rejections of claims 21 and 23, as well as rejecting new claims 31 and 33 for not being enabled.

Applicants are claiming a method of treating any and all diseases that are connected with a disorder of the immune system (claims 21, 23, and 33) and a method for treating any disease capable of being treated through the inhibition of cyclooxygenase (claim 31), and methods of treating many unrelated diseases, including Alzheimer's disease (claims 32 and 34).

The nature of the invention

The nature of the invention is of methods of treating immune system disorders/diseases, or diseases involving the COX-1 or COX-2 pathways, comprising administering a compound or a pharmaceutical composition to a patient in need thereof. The language of claims 21 and 23 encompasses any or all immune system disorders/diseases as well as any disease capable of being treated via the inhibition of cycolooxygenase.

The state of the prior art

The state of the prior art is that cyclooxygenase, or COX, (which exists as two isozymes, COX-1 and COX-2), is involved in the production of prostaglandins (PG), which play an important role in mediating pain and inflammation in thousands of diseases. The COX-1 enzyme is known to be implicated in diseases/disorders such as inflammation, edema, hyperalgesia, rheumatoid arthritis, arterial thrombosis, restenosis, erythema, rhinitis, asthma, cerebral infarction, blood coagulation disorders, respiratory tract diseases, etc. The COX-2 enzyme is involved in such diseases as inflammation, osteoarthritis, intestinal polyps, gastropathy, colorectal cancer, dysmenorrheal, ear edema, etc.

As stated previously, treating diseases "which are connected with a disturbance of the immune system" encompasses many diseases, including autoimmune and immunodeficiency diseases, for example MS, AIDS/HIV, SCID, CFS, and Alzheimer's, of which there is no known cure.

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of cyclooxygenase-mediated diseases, whether COX-1 or COX-2 was inhibited would affect the possible treatment of any disease. By Applicants' own admission, "the biochemical

mode of action of the two enzymes is not yet completely elucidated," (Specification, page 1). The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. In the absence of a showing of correlation between all the diseases claimed as capable of being treated by the compound of claim 1 and the inhibition of either or both cyclooxygenase enzymes, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 1.

The amount of direction or guidance present and

the presence or absence of working examples

The specification has enabled only the compounds according to formula (I) that selectively inhibit cyclooxygenase-1 and cyclooxygenase-2 enzymes. Treatment of the claimed distinct disorders/diseases are normally disease or symptom oriented, thus are highly individualized, i.e. treating the symptoms of eczema (itchy, inflamed skin) would not employ the same methods as treating the symptoms of rheumatoid arthritis (stiffness and joint pain). The direction present in the instant specification is that the compounds of claim 1 can inhibit the production of COX which helps in mediating pain and inflammation. However, the specification is silent and fails to provide guidance as to the complete list of immune system disorders or cyclooxygenase-mediated diseases, except for the brief list on page 14 that require the inhibition of COX, i.e. the specification fails to provide a correlation between all the diseases encompassed by the claims and the COX-1 or COX-2 enzyme.

There are no working examples for any diseases listed in the specification. Also, the compounds which are discloses in the specification have no pharmacological data regarding the treatment of any disease besides the inhibition of COX-1 in LPS-stimulated human monocytes *in*

vitro. Also, the specification fails to provide working examples as to how the listed diseases can be treated by the inhibition of COX, i.e. again, there is no correlation between the diseases listed and inhibition of COX. The standard of 35 USC 112, first paragraph rejections is that the application *itself* must inform, rather than direct, others to find out for themselves, please see *In re Garnder*, 166 USPQ 138.

The breadth of the claims

Applicants are claiming methods of treating a broad number of diseases that are unrelated. The allegation that the diseases claimed by the Applicants are all connected to the immune system or implicate the COX enzymes is insufficient support that the claimed compounds have specific efficacy in current available form for treating all of the diseases/disorders encompassed by the language of the claims. As stated above, the COX-1 enzyme is known to be implicated in inflammation, edema, hyperalgesia, rheumatoid arthritis, arterial thrombosis, restenosis, erythema, rhinitis, asthma, cerebral infarction, blood coagulation disorders, respiratory tract diseases, ischemia, necrosis, etc. The COX-2 enzyme is involved in such diseases as inflammation, osteoarthritis, intestinal polyps, gastropathy, colorectal cancer, dysmenorrhea, ear edema, barrett esophagus, colonic neoplasms, etc.

The quantity of experimentation needed

The quantity of experimentation needed is undue. One of ordinary skill in the art without direction, would be unable to treat each and every immune system disorder, and each and every disease benefited by the inhibition of COX, using the instant claimed compounds. One of skill in the art would need to determine what listed diseases would be benefited by the inhibition of the

cyclooxygenase pathway and would furthermore then have to determine whether the claimed compounds would provide treatment of all of the disease by the inhibition of COX-1 or COX-2.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity. As a result necessitating one of skill to perform an exhaustive search for which COX-mediated diseases can be treated by the compound of claim 1 in order to practice the claimed invention.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the claim 1 for the treatment of all disorders/diseases encompassed by the language of the instant claims. As a result, necessitating one of skill to perform an exhaustive search for which claimed diseases can be treated by the compound of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in

undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome by amending claims 21, 23, 31, and 33 to treat only the specific diseases listed in claims 32 and 34.

Conclusion

7. Claims 1-3, 5-7, 12-15, and 21-34 are pending, claims 21, 23, 31 and 33 stand rejected, and claims 1-3, 5-7, 12-15, 22, 24-30, 32, and 34 appear to be free of the prior art.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571.273.8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Coppins
March 31, 2006

KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER

Kamal Saeed

for Joseph K. McKane
SPE, Art Unit 1626